Medical Genetics Summaries

Providing actionable pharmacogenetic information pertaining to selected medical conditions

https://www.ncbi.nlm.nih.gov/books/NBK61999/

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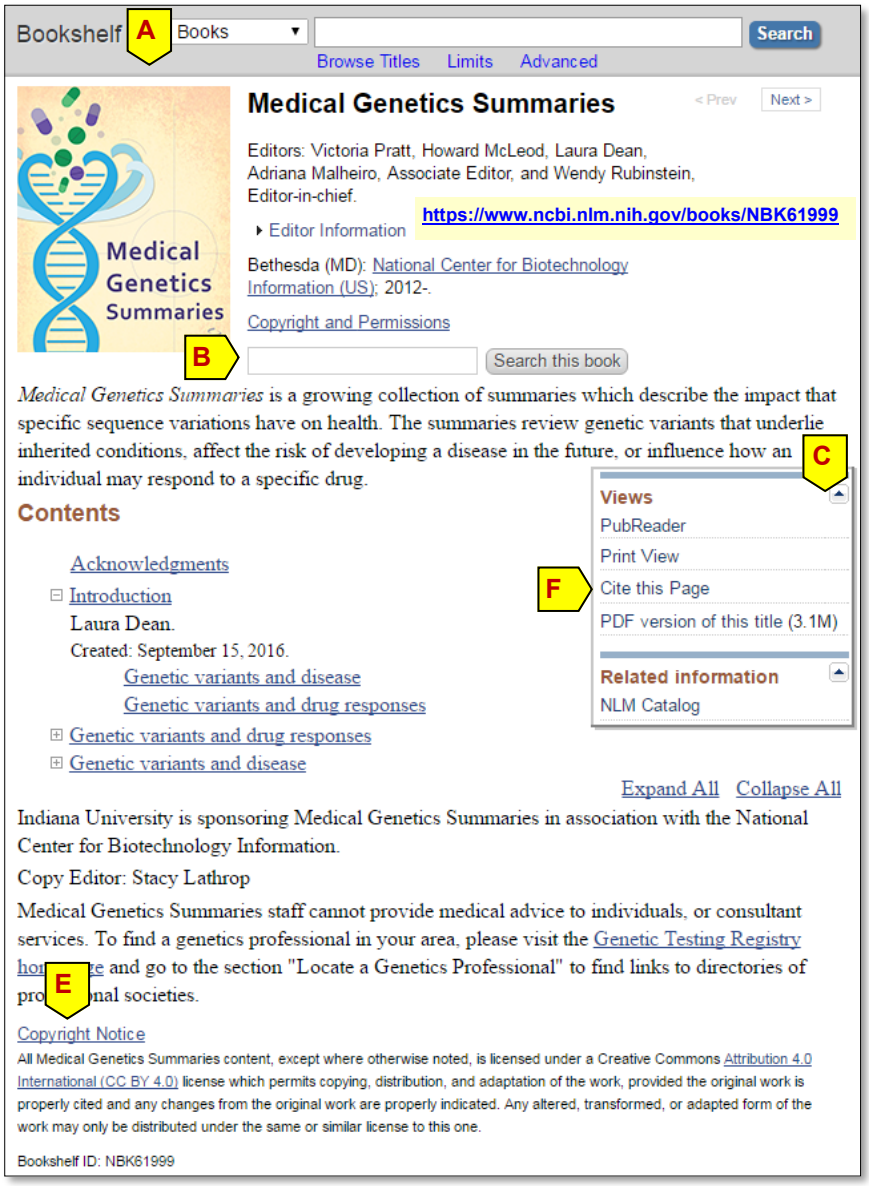
Introduction

Medical Genetics Summaries (MGS) helps the safe and effective prescribing of drugs. Created by NCBI, MGS provides actionable information on the dosing of drugs which are influenced by genetics. Each summary focuses on one drug and includes a description of the drug and its uses, the genes involved in the drug metabolism and efficacy, genetic testing strategies, therapeutic recommendations based on genotype, and nomenclature for the relevant alleles. New summaries are frequently added and every summary undergoes an extensive review process that includes peer review by an international team of clinical and pharmacogenetic experts.

The summaries contain regularly updated pharmacogenetic information from multiple authoritative sources, such as the FDA and professional practice guidelines. Because MGS content contains therapeutic recommendations in a structured format, it is ideally suited for integration in electronic health records (EHR) and hospital systems, and help clinicians who seek evidence-based information to use in clinical settings.

MGS integrates with other NCBI resources including ClinVar, dbSNP, DailyMed, MedGen and the NIH Genetic Testing Registry (GTR) and will continue to evolve to offer healthcare providers up to date medical and genetic testing information.



Access And Term of Use

MGS is freely available from the NCBI Bookshelf (**A**). The table of contents (partially collapsed) allows easy browsing of the drugs covered so far. The search box (**B**) enables searching with text terms related to the specific drug or gene of interest. The portlet in the upper right hand corner (insert, **C**) provides alternative display formats and a PDF download link. The whole book can be downloaded as a PDF, or individual chapters. Excerpts from MGS are also available in related records in GTR and MedGen (**D**).

No permission is required to reproduce/ redistribute the collection (**E**), but appropriate attribution should be given using the "Cite this Page" information (**F**).

Using MGS Service

An MGS summary can help clinicians to:

- order the most relevant genetic test
- interpret the genetic test results
- find therapeutic recommendations based on genetic test results
- learn about the pharmacogenetics of the drug
- explore related precision medicine resources

GTR, a database of orderable clinical genetic tests — https://www.ncbi.nlm.nih.gov/gtr

MedGen, a portal to phenotypes with a genetic component — https://www.ncbi.nlm.nih.gov/medgen

D

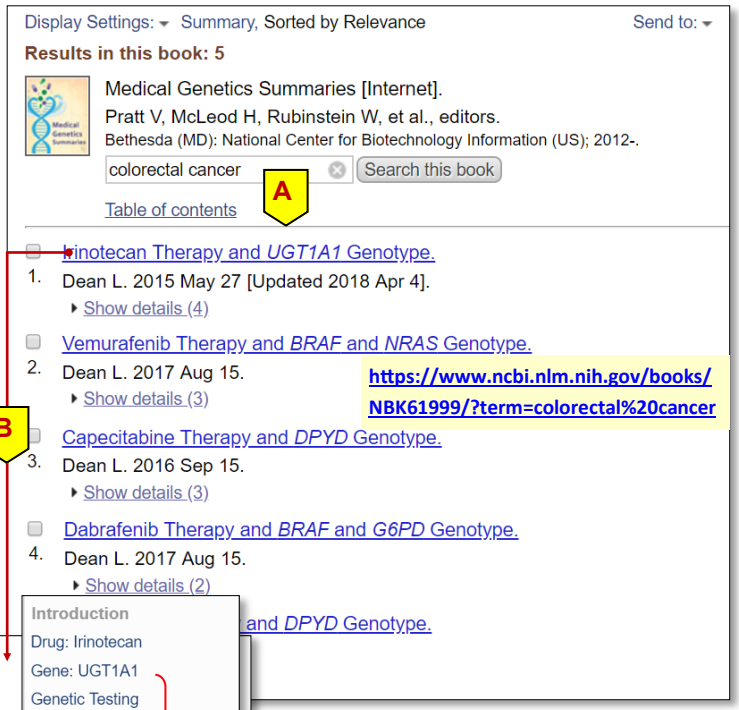
MGS Use Cases

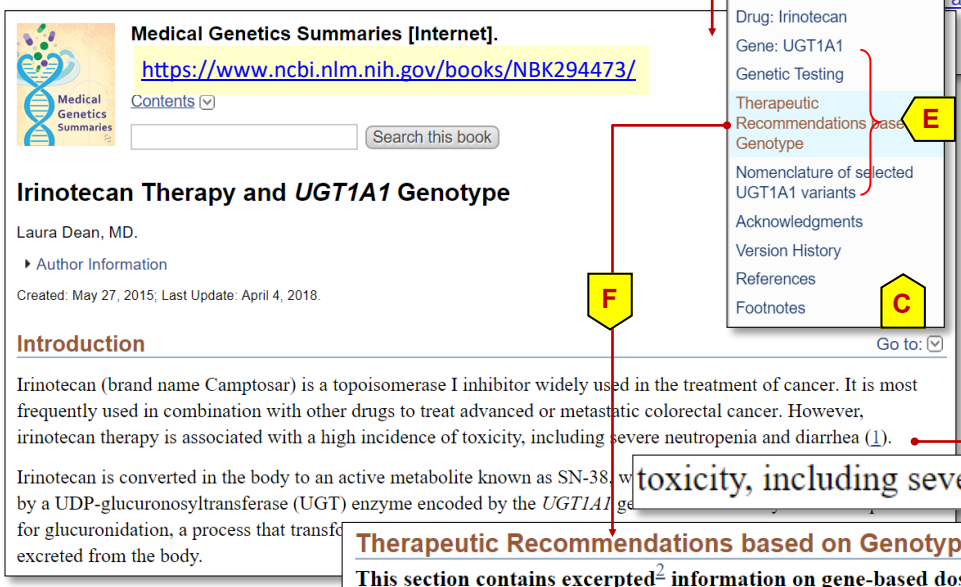
We will describe the uses of MGS by presenting a few examples.

Use Case 1: Find information about genetic testing to guide treatment for colorectal cancer

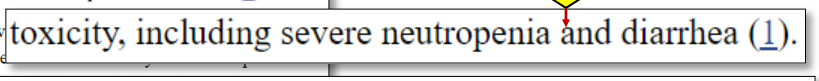
Searching MGS for "colorectal cancer" retrieves summaries for drugs used in colorectal cancer care. One such summary is "Irinotecan Therapy and *UGT1A1* Genotype" (**A**, with subsection links expanded).

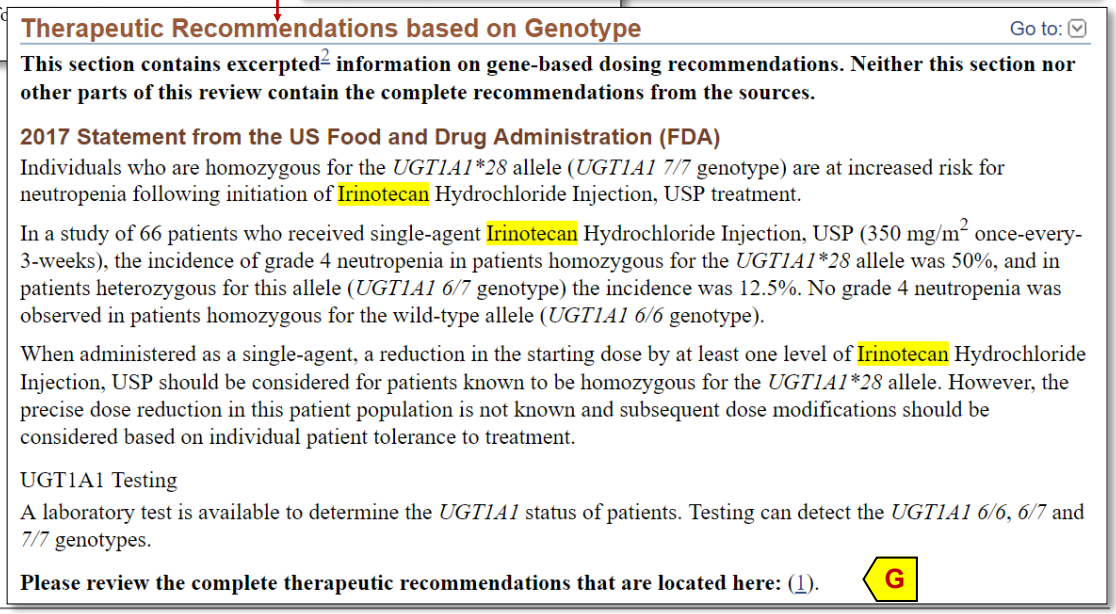
The title links to the entire content of this summary (**B**). In each summary, the "Go to" portlet on the right (insert, **C**) outlines its contents. All summaries have the same structured format, beginning with an introduction followed by dosing tables from the FDA and other authoritative guidelines. In this example, the summary is about irinotecan, a drug frequently used to treat metastatic colorectal cancer. Patients carrying certain variants of the *UGT1A1* gene have an increased risk of irinotecan toxicity, which includes severe neutropenia and diarrhea (**D**). For these patients, the starting dose of irinotecan should be reduced.





Separate sections of the summary are dedicated to the drug overview, information about the gene(s) that influence the safety and efficacy of the drug, genetic testing, therapeutic recommendations based on genotype, and the nomenclature used for genetic variants (**E**).



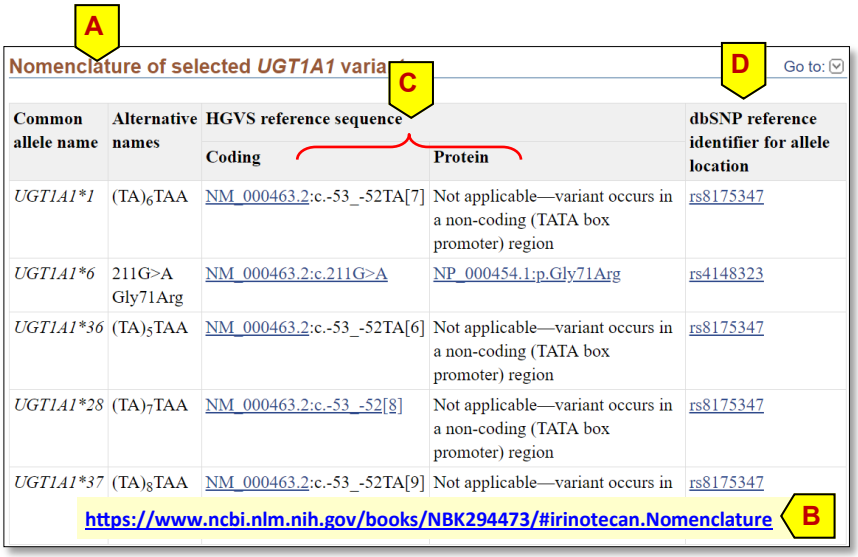


The "Therapeutic Recommendations" section (**F**) includes dosing recommendations from the FDA and authoritative guidelines, and provides links to the complete therapeutic recommendations (**G**).

MGS Use Cases (cont.)

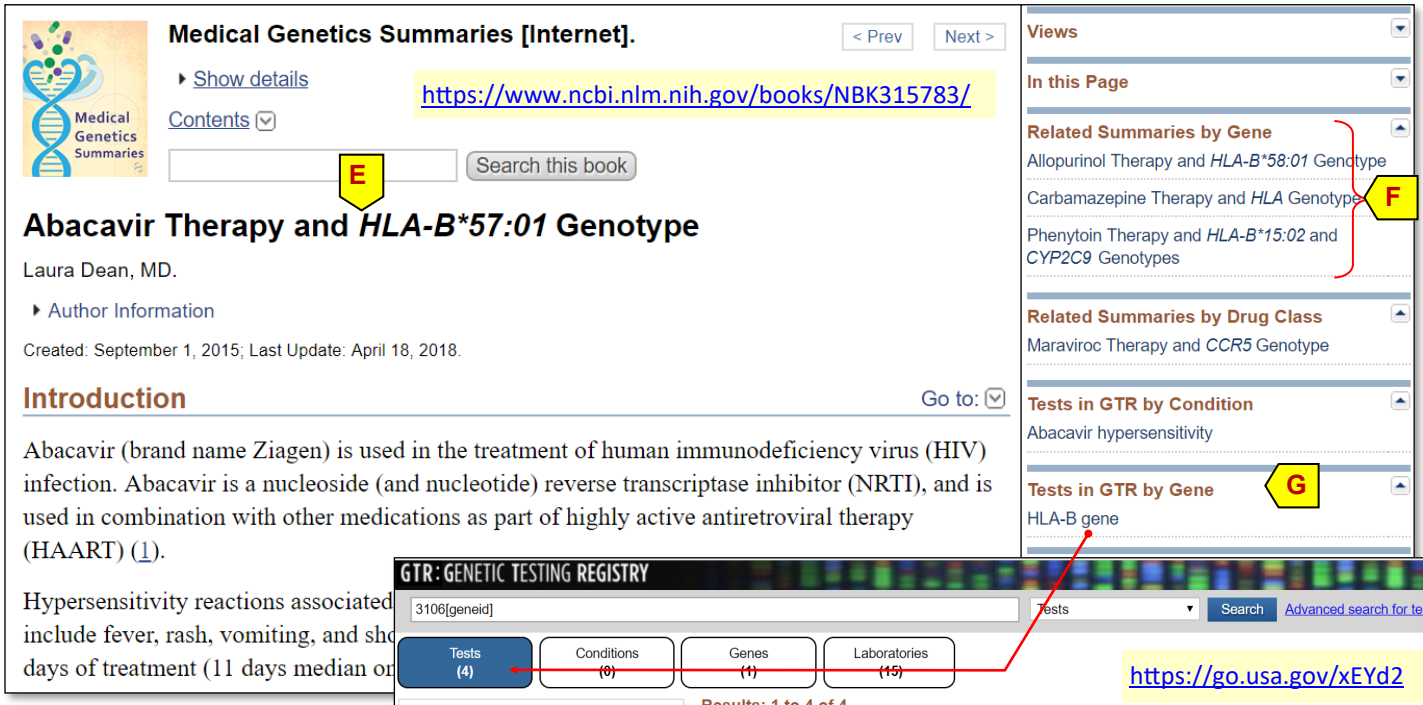
Use Case 2: Understand the nomenclature used for genetic variants

In the medical literature, genetic variants are sometimes described in different terms. In the nomenclature section, a table (**A**) matches the common variant names with the official HGVS expressions. Only the most common and/or significant alleles are listed here, but the table footnote includes a link to a comprehensive listing of all currently known variants (**B**). The table also links to the relevant records in ClinVar (**C**), and dbSNP (**D**), which allow for further investigation of the variants.



Use Case 3: Find tests for drug hypersensitivity risk factors in GTR.

The summary for the antiviral drug abacavir (brand name Ziagen) (**E**) states that *abacavir* is contra-indicated in individuals with a specific variant of the this *HLA-B* gene, known as *HLA-B*57:01*. This variant increases the risk of hypersensitivity to abacavir, which is a potentially fatal condition. Patients must be screened for *HLA-B*57:01* before starting abacavir therapy. Note: the *HLA-B* gene also impacts on the safety of other drugs. The "Related summaries by Gene" links (**F**) in the right column link to summaries for 3 such drugs.



The presence of *HLA-B*57:01* can be determined in several ways, including sequence analysis of the entire coding region. The "Tests in GTR by Gene" (**G**) links to tests related to the *HLA-B* gene that were voluntarily deposited in GTR by test providers (laboratories). The Filters allow for selections of relevant tests (**H**).

MGS Use Cases (cont.)

Use Case 4: Use GTR as a portal to further investigate precision medicine-focused data.

In addition to tests/laboratory information, GTR also lists conditions that are associated with an individual gene. In the same GTR test set discussed in Use Case 3, click the "Genes" button (**A**) to retrieve the list of conditions.

The individual conditions (**B**) link to the relevant records for the gene we are interested in (the HLA-B gene). Here, the GTR record for Abacavir hypersensitivity (**C**) displays an excerpt from MGS and links to the full MGS summary. In the right-hand column, the record also provides links to other relevant resources (**D**), such as the corresponding record in MedGen (**E**). The "Professional guidelines" section of the MedGen record lists recent publications on this subject, such as an abacavir dosing guideline (**F**) with its title linked to the abstract in PubMed (**G**). The right hand column (**H**) provides full-text links and links to similar articles for further exploration.